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RELATIONSHIP OF ANUG (ACUTE NECROTIC ULCERATIVE  
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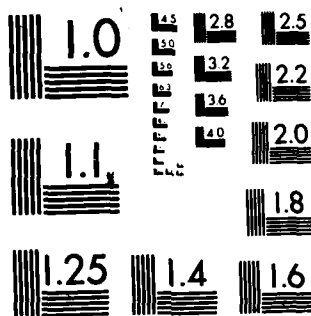
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Report Number 2

RELATIONSHIP OF ANUG, STRESS, AND LEUKOCYTE FUNCTION

ANNUAL SUMMARY REPORT

Ronald B. Cogen, Alvin W. Stevens,  
Steven Cohen-Cole and Katherine Kirk

October 22, 1981

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND  
Fort Detrick, Frederick, Maryland 21701

Contract No. DAMD 17-79-C-9176

University of Alabama School of Dentistry  
Birmingham, Alabama 35294

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Our second year in the study has thus far resulted in additional correlation of the first year's findings. The ANUG patients appear to be suffering from anxiety which may be correlated by a tendency for an increase in serum cortisol, and an increase in urine cortisol. Also it appears as though increased susceptibility to the microorganisms may be based on decreased lymphocyte and PMN function.			

### Summary:

Our second year in the study has thus far resulted in continuation and correlation of the reported first year findings. The ANUG patients appear to be suffering from anxiety which may be correlated by a tendency for an increase in serum cortisol, and an increase in urine cortisol. Also it appears as though increased susceptibility to the microorganisms may be based on decreased lymphocyte and PMN function.

### Foreward:

This is the second annual report, and I am happy to report that we have been able to exceed our first year milestone of 85 patients. We have been accumulating a wealth of data and analysis of this data has been encouraging that we are on the right track. It also is suggesting some new avenues for further investigation which may prove fruitful in our understanding not only of ANUG, but also other stress-related diseases and host-related defense mechanisms.

### Body of Report:

Some of our findings to date are as follows:

- (1) The patients were between 17-25 years of age. The youngest patient was 14 years old and the oldest was 33 years old. The mean age was 23.9 years old.
- (2) All of the patients with ANUG with the exception of one were caucasian. This suggests that there may be a genetic component and may be worth investigating. We feel that this may be an important uncovered component and was an unexpected finding.
- (3) The differential white blood cell counts were discontinued since all that were tested were within the normal range for all patients as well as controls.
- (4) The data from the psychologic testing instruments indicated that:
  - (a) Very Recent Life Changes - ANUG patients showed a significant difference ( $p=0.04$ ) in the subjective magnitude of recent life events, with patients rating their life changes as more severe.
  - (b) Dohrenwend's Life Events Scale - most significant differences between patients and controls occurred in the absolute number of reported negative life events ( $p=0.001$ ) and also the magnitude of the negative events.
  - (c) Social Support - preliminary analysis showed a nonsignificant trend for patients to rate their social support as lower than controls. More refined analysis will be attempted to separate some of the nuances revealed by sub-scales of this instrument.
  - (d) Spielberger State/Trait Anxiety Inventory - indicated a highly significant increase of State Anxiety in ANUG patients at T1 (upon presentation with the disease ( $p=0.0003$ )). This increase was not significant at T2. Also the Trait Anxiety of patients was significantly higher at T1 ( $p=0.0001$ ) compared to controls, but was only of border-line significance at T2.

- (e) General Health Questionnaire - this test correlates very well with diagnosis of emotional disorders by psychiatrists. When we use the suggested range of score of 5.0 or more on this scale we found that 67% of the patients compared to 21% of controls scored in the emotionally disorder range, which was significant at the 0.0001 level.
- (f) Center for Epidemiological Studies Depression Inventory indicated that 53% of the patients scored in the depressed range compared to 21% of the controls which also was significant ( $p=0.0006$ ).
- (g) Minnesota Multiphasic Personality Inventory which was tested at T2 (after resolution of the disease) indicated that patients had significantly elevated scores on both the Depression Scale and the Psychopathic Deviance Scale.

(5) Serum Cortisol Levels

There was a mean elevation of serum cortisol when comparing ANUG patients to controls which approaches statistical significance ( $p=0.07$ ) however interestingly if the serum cortisol levels are divided into quartiles, 64% of the ANUG patients fall into the upper one-half and 63% of the controls are in the lower one-half and these differences are significant ( $p=0.03$ )

(6) Urinary levels of Endocrine Markers of Stress

Overnight urine free cortisol levels were higher in ANUG patients at T1, and statistical evaluation indicates a trend but the differences were not statistically significant. However, at T2 the higher overnight urine free cortisol levels in patients compared to controls was statistically significant.

Other endocrine assessments to date, show no differences with respect to growth hormone, prolactin, total T4, total T3 and urine free catecholamines.

(7) Blood Leukocyte Function Assays

Much of the data generated during this second year has not yet been fully analyzed and is therefore far from complete

- (a) Phagocytosis - assessed by Stimulated NBT test - the mean average depression of ANUG patients compared to controls was 21% and this mean depression is significant ( $p=0.0043$ )
- (b) Leukotaxis - assessed with modified Boyden chamber using a filtrate of E. coli as the attractant. There was an average depression in ANUG patients of 26% compared to controls after correcting for non-stimulated migration. The difference in means was statistically significant at the 0.0036 level.
- (c) Lymphocyte function was assessed by response to non-specific mitogens. With use of Con A there was a 60% decrease in ANUG patients compared to controls which was significant at the 0.0001 level to corroborate this we have substituted PWM for PHA however the results of these assays have not been tabulated as yet.

In summary, the basis of this preliminary data, it appears that several psychosocial variables are strongly associated with ANUG. Also, three of the four measures of immune functions were depressed in ANUG patients when

compared to controls and the fourth assay showed a trend. The veracity of this trend is being examined by substituting another assay. The extreme paucity of black patients with ANUG has continued through the second year of the study and is highly suggestive of an important genetic component to this disease which is worthy of further exploration. These findings, to date, suggest that genetic, psychosocial, endocrine, and immune variables may all play a role in the pathogenesis of this illness. We hope in the future to be able to design prospective studies to help clarify the relative importance and relative independence of these various factors.

As a result of the work to date three reports have been made to National Meetings.

1. American Association of Psychosomatic Medicine
2. International College of Psychosomatic Medicine
3. American Academy of Periodontology

The above abstracts have been included with this report.

In addition, 2 abstracts have been forwarded to the International Association for Dental Research and a manuscript entitled Psychosocial and Endocrine Aspects of Acute Necrotizing Ulcerative Gingivitis has been sent to the Journal of Psychosomatic Medicine. Also two more manuscripts are being prepared for submission to the Journal of Periodontology

Upon acceptance the above will be forwarded to you.



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